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PATENT SPECIFICATION

NO DRAWINGS

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COMPLETE SPECIFICATION

Improvements relating to Carbohydrate-Derived Polymers

We, THE MILK MARKETING BOARD, a British body corporate established by statute, of Thames Ditton, Surrey, Great Britain, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to the preparation of carbohydrate-derived synthetic polymers and derivatives thereof. In particular the invention relates to synthetic linear polymers formed from esters of α,β unsaturated polymerisable acids and galactose.

It is known to synthesise high molecular weight polymers by treating unsaturated compounds, such as methyl methacrylate and acrylate, with free-radical catalysts. It is further known to synthesise high molecular weight polymers containing carbohydrate residues by treating suitably substituted carbohydrate methacrylates and acrylates with free-radical catalysts. Examples of such sugar monomers are 1,2:5,6-di-*O*-isopropylidene-3-*O*-methacryloyl- α -*D*-glucofuranose (Black, Dewar and Rutherford, J. Chem. Soc., 1963, 4433; Kimura and Imoto, Makromol. Chem., 1961, 50, 155) and 3-*O*-acryloyl - 1,2:5,6 - di - *O* - isopropylidene- α - *D* - glucofuranose (Fisher and Harper, US Patent No. 3,103,508). In preparing these monomers, all but one of the hydroxyl groups of glucose are first reacted with acetone to form the 1,2:5,6-diketal, and the remaining alcohol group on position 3 is then reacted to give the unsaturated ester, which is polymerisable to soluble, fusible products. If glucose is reacted directly with the unsaturated esterifying reagent without prior treatment with acetone, a polyfunctional sugar monomer results, and such compounds cross-link during polymerisation to give hard, brittle, intractable resins, which have no utility.

The importance of carbohydrate-derived polymethacrylates and polyacrylates lies in the fact that the acetone blocking groups can be selectively removed by treatment with acid to yield water-soluble, high molecular weight colloids of outstanding industrial potential. Thus, poly(di-*O*-isopropylidene-3-*O*-methacryloyl- α -*D*-glucofuranose) is converted by hydrochloric acid into the water soluble poly(3-*O*-methacryloyl-*D*-glucose) (Black *et al.*, loc. cit.). Unlike normal polysaccharides of plant, animal and microbial origin, this synthetic polymer has its reducing group at position 1 free in every glucose unit and so is much more reactive than polysaccharides wherein only the reducing group at the end of the chain is free.

The present invention relates to several improvements in the production of carbohydrate-derived synthetic polymers and derivatives thereof having exceptional commercial promise. More particularly, this invention relates in one major aspect to synthetic polymers containing substituted or unsubstituted *D*-galactose residues. A second major aspect of this invention relates to a process for removing the acetone blocking groups from the substituted galactose polymers.

According to the present invention a method of preparing a polymer from esters of α,β olefinically unsaturated polymerisable aliphatic mono- and di-carboxylic acids and galactose comprises reacting a ketone with galactose to form a 1,2:3,4 diketal, forming an ester of said diketal and an α,β olefinically unsaturated polymerisable aliphatic mono- or di-carboxylic acid, polymerising said ester in the presence of a free

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radical catalyst and finally removing the diketal residues from the polymerised product by controlled hydrolysis.

Preferably the controlled hydrolysis is effected by dissolving the polymerised product in an organic acid and diluting the solution gradually with water. Preferably the organic acid is formic acid.

Suitable α,β olefinically unsaturated aliphatic mono- and di-carboxylic acids include acrylic, methacrylic, α -chloroacrylic, α -cyanoacrylic, maleic, half esters of maleic, fumaric, half esters of fumaric, α -ethacrylic, itaconic and half esters of itaconic. The preferred acids are acrylic and methacrylic.

Suitable ketones include acetone, methyl ethyl ketone, methyl propyl ketone, mono-chloroacetone and cyclohexanone. The preferred ketone is acetone.

The free radical catalyst is preferably azobisisobutyronitrile.

The aforesaid ester may be formed by reacting the diketal with a lower hydrocarbon ester of the α,β olefinically unsaturated acid in the presence of a vinyl polymerisation inhibitor and a catalyst, and distilling off hydrocarbon alcohol from the reaction mixture as it is formed. Said "lower hydrocarbon ester" may be a methyl, ethyl, propyl, butyl, or amyl ester.

Alternatively, the ester may be prepared by reacting the diketal with an anhydride of the α,β unsaturated acid.

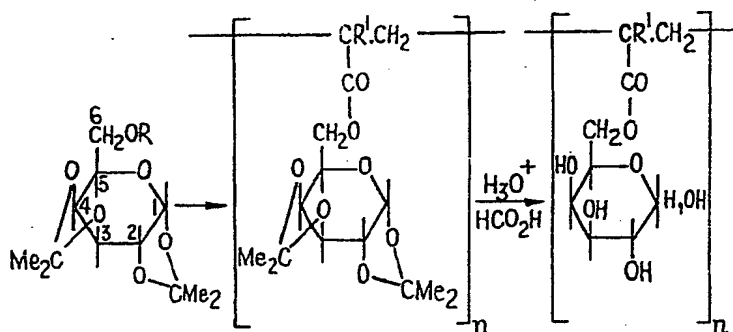
The present invention is also a polymer of an ester between the hydroxyl group in the 6 position of galactose and an α,β unsaturated polymerisable acid.

Specific examples of the invention are poly(galactose 6-methacrylate), poly(galactose 6-acrylate) and derivatives thereof.

We have discovered that polymers derived from galactose monomers possess higher molecular weights than those of polymers synthesised from most other sugar monomers. This is attributed, at least in part, to the fact that the monofunctional, polymerisable galactose compounds of this invention are well-defined, crystalline derivatives, which can be obtained in a high degree of purity by repeated recrystallisation.

We have also discovered that the high molecular weight polymers derived from galactose are deacetonated with difficulty, if at all, by treatment with hydrochloric or other aqueous mineral acid, but that deacetonation is readily effected by dissolving the acetonated polymers in an anhydrous organic acid, preferably formic acid, and gradually diluting the solution with water, whereby the protecting acetone groups are slowly hydrolysed off, leaving the water-soluble, high molecular weight, deacetonated polymers.

Typical reactions within the scope of this invention may be represented structurally as follows:—



(I: R = H)

(II: R = Co.CMe:CH₂)

(V: R = CO.CH:CH₂)

(III: R¹ = Me)

(VI: R¹ = H)

(IV: R¹ = Me)

(VII: R¹ = H)

For viscosity measurements, n is probably in the region of several hundred and may be as high as 1000, and the molecular weights of the polymers may be of the order of several hundred thousand.

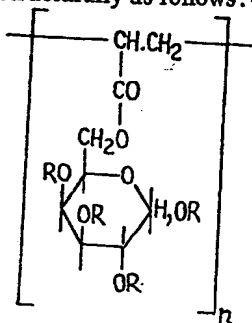
The well-known compound, 1,2:3,4-di-O-isopropylidene- α -D-galactopyranose (I), known hereafter as diisopropylidene-galactose, is esterified with methacrylic anhydride in pyridine solution to give the pure, crystalline 6-methacrylate (II). Monomer (II) is polymerised in bulk or in benzene solution with azobisisobutyronitrile or other

free-radical catalyst and the acetonated product (III) purified by solution in chloroform and reprecipitation with methanol. Solution of polymer (III) in formic acid and careful addition of water remove the acetone groups, and the novel synthetic polymer (IV) is isolated after dialysis.

The pure, crystalline 6-acrylate (V) is synthesised by transesterification between ethyl acrylate and diisopropylidenegalactose in accordance with the teaching of U.S. Patent No. 3,103,508 for the corresponding glucose monomer. Compound (V) is polymerised and deacetonated to give polymer (VII).

We have also discovered that the novel, water-soluble poly (galactose methacrylate) (IV), can be esterified with well-known reagents to give derivatives with potentially useful properties. Typical reactions within the scope of this invention include acetylation, benzylation, phenylcarbamoylation, and nitration. Acetylation of polymer (IV) in dimethylformamide solution with acetic anhydride-pyridine affords the polymer acetate with a degree of substitution (D.S.) of 3.65 and with a high inherent viscosity (5.2 dl/g in tetrachloroethane). Benzylation with benzoyl chloride in the presence of pyridine gives a benzoate with a D.S. of 2.7 and an inherent viscosity of 9.3 dl/g (in tetrachloroethane). Treatment of polymer (IV) in dimethylformamide solution with phenylisocyanate at 100° yields the triphenylcarbamate derivative in good yield. Nitration of polymer (IV) with nitrogen pentoxide in chloroform gives an insoluble trinitrate.

Similarly, poly(galactose acrylate) (VII), also gives rise to potentially useful derivatives on esterification, although with this polymer higher degrees of substitution are obtainable. The acetate, benzoate, and phenylcarbamate had a D.S. of 3.6, 3.7, and 3.6 respectively, which shows that almost complete substitution is attained. These derivatives may be represented structurally as follows:—

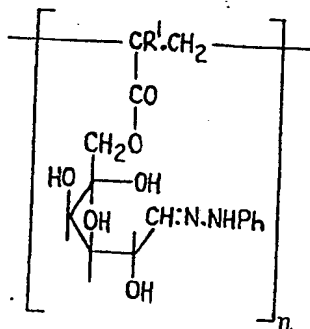


For the tetraacetate: $\text{R} = \text{CH}_3 \cdot \text{CO}$

„ „ tetrabenzoate: $\text{R} = \text{C}_6\text{H}_5 \cdot \text{CO}$

„ „ tetraphenylcarbamate: $\text{R} = \text{C}_6\text{H}_5 \cdot \text{NH} \cdot \text{CO}$

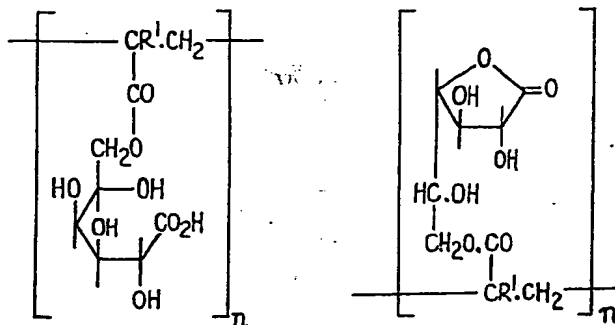
A further important class of derivatives of polymers (IV) and (VII) can be prepared by reaction of the reducing group at carbon atom 1 with various reagents. As aforesaid such reactions are impossible with natural polysaccharides of plant, animal and microbial origin, because with natural polymers only the reducing group at the end of each polymer molecule is free for reaction, all the remaining glycosidic hydroxyl groups being linked in acetal formation to give the polymer chain. As an example of this type of derivative, phenylhydrazine in acetic acid reacts with polymers (IV) and (VII) in dimethylformamide solution to give the fully substituted polymeric phenylhydrazones (VIII) and (IX) in high yield:



(VIII: R' = Me)
(IX: R' = H).

A phenylosazone derivative of polymers (IV) and (VII) is prepared by heating an aqueous solution of the polymer with phenylhydrazine and acetic acid, but analysis reveals that only one in every three galactose units is substituted as the phenylosazone, the other to remaining as the phenylhydrazone.

Another novel reaction exhibited by poly(galactose methacrylate) (IV) and poly(galactose acrylate) (VII) is oxidation at carbon atom 1. Chlorous acid at pH 3 converts polymer (IV) initially into poly(6-O-methacryloyl-D-galactonic acid) (X), which on isolation and drying loses a molecule of water to give the water-insoluble polymeric 1,4-lactone (XI).



(X: R' = Me)

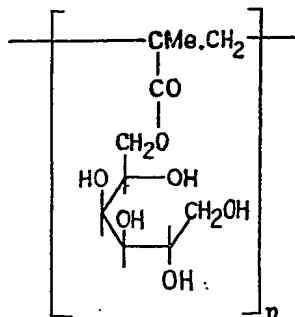
(XII: R' = H)

(XI: R' = Me)

(XIII: R' = H)

Similarly, chlorous acid oxidation of polymer (VII) gives the acid (XII) and its 1,4-lactone (XIII). These polyacids (X) and (XII) resemble the industrially important, naturally occurring pectic and alginic acids. On being neutralised with an alkali metal hydroxide, such as sodium hydroxide, they give extremely viscous solutions in water, which become much less viscous on addition of an electrolyte, such as sodium chloride, which suppresses ionisation of the macromolecule. These salts are thus typical polyelectrolytes, which constitute an industrially useful class of compounds. Among high-molecular-weight polyelectrolytes that are used extensively in industry, one may cite sodium alginate, sodium pectate, carrageenan, and many other gums and mucilages containing acidic groups. Polyacids (X) and (XII) also resemble pectic and alginic acids in forming insoluble salts with many metal cations. They differ, however, in lactonising much more readily than pectic and alginic acids.

The reducing group at carbon atom 1 of poly(galactose methacrylate) (IV) is readily reduced with sodium borohydride in aqueous solution to give poly(6-O-methacryloyl-D-galactitol) (XIV) in high yield:—



(XIV)

This polymer has a high inherent viscosity and is non-reducing. It gives a tetranitrate on nitration with nitrogen pentoxide in chloroform, which is partially soluble in ethyl acetate.

The following examples show embodiments of this invention with the under-

standing that the examples are illustrative only. It should be appreciated that changes in the reaction conditions will produce different degrees of substitution, inherent viscosities, and specific rotations. The degree of substitution can be varied at will as in the case of natural polysaccharides, such as cellulose, starch, alginic acid, etc.

The following examples show embodiments of this invention.

EXAMPLE 1.

Preparation of Diisopropylidenegalactose (I).

Eleven and a half grams of anhydrous galactose, 25 g of anhydrous copper sulphate, 250 ml. of anhydrous acetone, and 1.25 ml. of concentrated sulphuric acid were shaken for 24 hr. at 20°, the copper sulphate filtered and washed with acetone, and the filtrate and washings neutralised by shaking with 12 g of powdered calcium hydroxide for 18 hr. The solids were filtered and washed with acetone, and the filtrate and washings concentrated and distilled in a high vacuum. The colourless, viscous syrup which boiled at 100°/0.04 mm. amounted to 12.6 g (75.9% yield) and was identified as diisopropylidenegalactose (I), $[\alpha]_D - 57.4^\circ$ (2 g./100 ml. in chloroform).

Anal.: C, 55.6; H, 7.9. Calc. for $C_{12}H_{20}O_6$: C, 55.4; H, 7.75%.

Preparation of Diisopropylidenegalactose 6-methacrylate (II).

A solution of 26.8 g of diisopropylidenegalactose (prepared as described above) in 135 ml. of anhydrous pyridine was heated at 65° for 3.5 hr. with 27 ml. of methacrylic anhydride. A hundred and thirty-five ml. of water were then added, the solution heated at 65° for 1 hr. and at 30° for 17 hr., and the mixture extracted three times with 50 ml. each of light petroleum (b.p. 30–40°). The petroleum extracts were washed three times with 140 ml. each of water and three times with 140 ml. of 5% sodium bicarbonate solution, dried with anhydrous sodium sulphate, and filtered. Tetrachlorohydroquinone (28 mg.) was added to the filtrate and the petroleum was stripped off under reduced pressure. The resulting white solid was recrystallised from a mixture of 140 ml. of ethanol and 100 ml. of water, and the white crystals of pure diisopropylidenegalactose 6-methacrylate (II) weighed 16.1 g. (47.5% yield) and had a melting-point of 62.5–63° and a specific rotation of -49.2° (1.13 g./100 ml. in chloroform).

Anal.: C, 58.4; H, 7.42. Calc. for $C_{16}H_{27}O_7$: C, 58.5; H, 7.36%.

Polymerisation of Diisopropylidenegalactose 6-Methacrylate.

Ten grams of Diisopropylidenegalactose 6-methacrylate (prepared as above), 20 mg. of azobisisobutyronitrile, and 2.5 ml. of rigorously de-oxygenated benzene were heated at 50° for 24 hr. in a glass stoppered flask. The polymerised product was dissolved in 400 ml. of chloroform and the solution dripped slowly with stirring into 4 litres of methanol. The supernatant was decanted and the white precipitate of poly-(diisopropylidenegalactose methacrylate) (III) washed thoroughly by decantation with methanol. The dry polymer weighed 9.50 g. (95% yield) and had $[\alpha]_D - 54^\circ$ (0.5 g./100 ml. in tetrachloroethane). The inherent viscosity was 2.82. dl./g. (0.5 g./100 ml. in tetrachloroethane, 25°). Anal.: C, 59.1; H, 7.40. Calc. for $(C_{16}H_{24}O_7)_n$: C, 58.5; H, 7.36%.

Preparation of Poly(galactose methacrylate) (IV).

An amount of 3.3 g of the poly(diisopropylidenegalactose methacrylate), prepared as above, was dissolved at 20° in 396 ml. of formic acid and 24 ml. of water added. The solution was stirred at 20° for 22 hr. when the specific solution was +59°, (calculated on weight of acetonated polymer (III)). A further 180 ml. of water was then added and the solution stirred for 3 hr. The rotation ($[\alpha]_D + 58^\circ$) was now constant, thus indicating that hydrolysis of the acetone groups was complete. The solution was dialysed against running water until free from formic acid, concentrated under reduced pressure to small volume, and freeze-dried. The resulting white powder of poly(galactose methacrylate) (IV) weighed 2.42 g (96.8% yield) and exhibited $[\alpha]_D + 62.4^\circ$ (0.5 g./100 ml. in water). A quantitative determination of reducing power with sodium hypoiodite gave a value of 91.2%. Anal.: C, 48.75; H, 6.58. Calc. for $C_{10}H_{16}O_7$: C, 48.4; H, 6.50%. Its inherent viscosity in water was 1.91 dl./g. (0.5 g./100 ml.; 25°). Polymer (IV) was soluble in water and dimethylsulphoxide but insoluble in most common solvent.

EXAMPLE 2.

Preparation of Diisopropylidenegalactose 6-Acrylate (V).

Five and a half grams of diisopropylidenegalactose (prepared as described in

Example 1), 33 ml. of ethyl acrylate, 1.1 g of p-methoxyphenol, and 1.1 ml. of tetra-isopropyl titanate were heated at 110° for 2 hr. with stirring in an atmosphere of nitrogen. During the course of the transesterification, 15 ml. of ethyl acrylate-ethanol azeotrope were collected as distillate. A volume of 4 ml. of water and 20 ml. of light petroleum (b.p. 60—80°). were then added to the refluxing mixture, which was then allowed to cool to 20°. The gelatinous titanium dioxide was centrifuged, washed three times with 20 ml. each of petroleum, and the supernatant and washings washed three times with 50 ml. of water, three times with 50 ml. of 0.5 N-potassium hydroxide, and finally three times with 50 ml. of water. After the petroleum was stripped off under reduced pressure, the resulting syrup was dissolved in 20 ml. of methanol and 10 ml. of water added to produce a slight turbidity. The solution was kept overnight at 0° when an orange-red oil deposited. On decantation the supernatant crystallised immediately. After overnight at 0°, the white crystalline mass was washed twice with 10 ml. portions of methanol-water mixture (1:1 by volume) and dried. The crystals of pure diisopropylidenegalactose 6-acrylate (V) weighed 2.69 g. (40.6% yield). The mother liquor was concentrated and the solid recrystallised from a mixture of 10 ml. of methanol and 5 ml. of water to give 0.80 g of a second crop. The total yield was 52.6%. The compound (V) had a melting-point of 57.5° and a specific rotation of -50.2° in chloroform (1 g./100 ml.). Anal.: C, 57.5; H, 7.02. Calc. for $C_{15}H_{22}O_7$: C, 57.3; H, 7.05%.

For polymerisation experiments, the ester (V) was recrystallised three times from a mixture of methanol and water.

Polymerisation of Diisopropylidenegalactose 6-Acrylate.

Ten grams of the diisopropylidenegalactose 6-acrylate, prepared as above, 20 mg. of azobisisobutyronitrile, and 2.5 ml. of oxygen-free benzene were heated at 50° for 24 hr. in a glass-stoppered flask. The polymerised product was worked up exactly as described in Example 1. The dry poly(diisopropylidenegalactose acrylate) (VI) weighed 9.10 g. (91% yield) and had $[\alpha]_D -50.1^\circ$ in tetrachloroethane (0.5 g/100 ml.). Its inherent viscosity was 0.91 dl./g. in tetrachloroethane (0.5 g./100 ml.; 25°). Anal.: C, 57.6; H, 7.05. Calc. for $(C_{15}H_{22}O_7)_n$: C, 57.3; H, 7.05%.

Preparation of Poly(galactose acrylate) (VII).

An amount of 8.8 g of poly(diisopropylidenegalactose acrylate), prepared as above, was dissolved at 20° in 1, 160 ml. of anhydrous formic acid and 70 ml. of water added. To this solution during two and a half hr., quantities of water (total volume 530 ml.) were added at half hourly intervals and the solution stirred for 3 days, when the specific rotation was constant at +53° (calculated on weight of acetonated polymer (VI)), thus indicating that hydrolysis was complete. The final solution was dialysed against running water, concentrated under reduced pressure to small volume and freeze-dried to yield poly(galactose acrylate) (VII) as a white powder. The weight was 6.90 g. (109% yield). The specific rotation in water was +56.3° and the inherent viscosity in water was 0.58 dl./g. (0.5 g/100 ml.; 25°). A quantitative determination of reducing power with sodium hypoiodite gave a value of 90.9%. Anal.: C, 45.3; H, 6.04. Calc. for $(C_6H_{14}O_7)_n$: C, 46.15; H, 6.02%. Polymer (VII) was soluble in water, dimethylsulphoxide and N-methyl-2-pyrrolidene, but insoluble in most common solvents.

The polymers prepared as herein set forth are useful as sizing agents and thickeners.

EXAMPLE 3.

Acetylation of Poly(galactose methacrylate) (IV).

One gram of poly(galactose methacrylate) (IV), prepared as described in Example 1, was dissolved in 100 ml of dimethylformamide and treated with 12 ml of pyridine and 24 ml of acetic anhydride at 20° for 24 hr. The solution was added dropwise to water and the white precipitate was centrifuged and washed with water. The dry product, weighing 1.37 g. was dissolved in 25 ml of pyridine and the solution shaken with 50 ml of acetic anhydride at 20° for 24 hr. The product was isolated by pouring into water and purified by reprecipitation of a dimethylformamide solution with water. The polymer acetate was washed thoroughly with water and dried to a white powder, weighing 1.335 g and having $[\alpha]_D +47^\circ$ (0.5g/100 ml in tetrachloroethane). Its inherent viscosity in tetrachloroethane was 5.2 dl/g (0.5 g/100 ml at 25°). Anal.: C, 51.6; H, 5.84; Ac, 39.1. Calc. for $(C_{10}H_{12.5}O_7Ac_{3.5})_n$: C, 51.7; H, 5.85; Ac, 39.1%. The yield (82.6%) was calculated on this formula, i.e. degree of substitution (D.S.) = 3.65.

Benzoylation of Poly(galactose methacrylate) (IV).

A quantity of 252 mg of poly(galactose methacrylate) (IV) was dissolved in 25 ml of dimethylformamide and 5 ml of pyridine added. The mixture was cooled to 0° and 2.5 ml of benzoyl chloride added dropwise, and the solution kept for 7 days at 20° with occasional shaking. The red solution was added dropwise with stirring to ice-water, and the sticky precipitate washed with water and hardened with methanol. The product was dissolved as far as possible in 50 ml of acetone and the insoluble gel removed by centrifuging. The viscous supernatant was added dropwise with stirring to water and the precipitate washed and dried. The white polymer benzoate, weighing 422 mg, had $[\alpha]_D + 100 \pm 5^\circ$ (0.1 g/100 ml in tetrachloroethane) and the inherent viscosity was 9.3 dl/g (0.1 g/100 ml in tetrachloroethane at 25°). Anal.: C, 65.5; H, 4.86. Calc. for $C_{10}H_{13.5}O_7Bz_{2.7}$: C, 65.6; H, 5.10%. The yield was 78.6% based on this formula (D.S. = 2.7).

Phenylcarbamoylation of Poly(galactose methacrylate) (IV).

A quantity of 0.4 g of poly(galactose methacrylate) (IV) was dissolved in 20 ml of dimethylformamide, 2 ml of phenyl isocyanate added, and the solution heated at 100° for 3 hr. The product was precipitated with ethanol, washed with ethanol and ether, and again treated with 20 ml of dimethylformamide and 2 ml of phenyl isocyanate as before. The phenylcarbamate was purified by solution in 100 ml of acetone and reprecipitation with 400 ml of light petroleum (b.p. 40–60°). The light-brown triphenylcarbamate, weighing 845 mg (82.8% yield), had $[\alpha]_D + 20^\circ$ (0.1 g/100 ml in tetrachloroethane) and an inherent viscosity of 1.3 dl/g (0.1 g/100 ml in tetrachloroethane at 25°). Anal.: C, 61.9; H, 5.08; N, 7.2. Calc. for $(C_{11}H_{11}N_2O_{10})_n$: C, 61.5; H, 5.2; N, 6.9%. The yield was based on this triphenylcarbamate formula (D.S. = 3).

Nitration of Poly(galactose methacrylate) (IV).

A solution of 1.32 g of nitrogen pentoxide in 10 ml of chloroform, prepared as described by Caesar and Goldfrank (J. Amer. Chem. Soc., 1946, 68, 372), was placed in a beaker, fitted with a thermometer and stirrer, and 0.2 g of sodium fluoride added. The reagents were cooled to -10°, and when the temperature had risen to 0° 211 mg of poly(galactose methacrylate) (IV) was added. The temperature rose immediately to 4° and stirring was continued for 45 min. when the final temperature was 10°. The product was washed with chloroform and hot water, and dialysed against running water for 3 days. The insoluble trinitrate was isolated as a white powder, weighing 285 mg (87.4% yield). Anal.: C, 30.0; H, 3.20; N, 10.5. Calc. for $(C_{10}H_{11}O_{13}N_3)_n$: C, 31.3; H, 3.42; N, 11.0%. The yield was calculated on this trinitrate formula (D.S. = 3).

EXAMPLE 4.

Acetylation of Poly(galactose acrylate) (VII).

A quantity of 303 mg of poly(galactose acrylate), prepared as described in Example 2, was dissolved in 30 ml of dimethylformamide and 3.6 ml of pyridine, and 7.2 ml of acetic anhydride added. The solution was kept at 20° for 24 hr. and then added dropwise to ice-water with stirring, and the precipitate washed with water and dried. The product was redissolved in 8 ml of pyridine and again acetylated as before with 16 ml of acetic anhydride. The polymer acetate was purified by solution in 40 ml of chloroform and reprecipitation in 200 ml of light petroleum (b.p. 40–60°) and finally isolated as a white powder, weighing 420 mg, with a D.S. of 3.6. It had $[\alpha]_D + 52^\circ$ (0.5 g/100 ml in tetrachloroethane) and an inherent viscosity of 0.9 dl/g (0.5 g/100 ml in tetrachloroethane at 25°). Anal.: C, 50.8; H, 5.38; Ac, 40.1. Calc. for $(C_9H_{10.4}O_7Ac_{3.6})_n$: C, 50.5; H, 5.54; Ac, 40.2%.

Benzoylation of Poly(galactose acrylate) (VII).

A quantity of 207 mg of poly(galactose acrylate) was dissolved in 20 ml of dimethylformamide and 4 ml of pyridine, the solution cooled to 0°, and 2 ml of benzoyl chloride added dropwise with stirring. The solution was left at 20° for 7 days, when it was added dropwise to ice-water to give a sticky precipitate, which was hardened with methanol. The benzoate was dissolved in 50 ml of chloroform and reprecipitated with 250 ml of light petroleum (b.p. 40–60°) to yield a white powder, weighing 368 mg (67.3% yield), which had $[\alpha]_D + 94^\circ$ (0.5 g/100 ml in tetrachloroethane) and an inherent viscosity of 1.5 dl/g (0.5 g/100 ml in tetrachloroethane at 25°). Anal.: C, 67.7; H, 5.26. Calcd. for $(C_9H_{10.3}O_7Bz_{3.7})_n$: C, 67.7; H, 4.69%. The D.S. was 3.7.

Phenylcarbamoylation of Poly(galactose acrylate) (VII).

A quantity of 0.2 g of poly(galactose acrylate) was dissolved in 10 ml of dimethylformamide, 1 ml of phenyl isocyanate added, and the solution heated at 100° for 3 hr. The cooled solution was added to 100 ml of isopropanol and the precipitate coagulated with 20 ml of ether. The product was again reacted with the same amounts of dimethylformamide and phenyl isocyanate, and the phenylcarbamate finally purified by solution in 40 ml of dimethylformamide and reprecipitation in ten volumes of ice-water. The pure compound was a white powder, weighing 352 mg (62.2% yield), with $[\alpha]_D + 30^\circ$ (0.52 g/100 ml in dimethylformamide), inherent viscosity of 1.0 dl/g (0.52 g/100 ml in dimethylformamide), and D.S. of 3.6. Anal.: C, 61.9; H, 5.09; N, 7.6. Calc. for $[C_9H_{14}O_7(PhNCO)]_n$: C, 61.9; H, 4.87; N, 7.6%.

EXAMPLE 5.

Preparation of Phenylhydrazone of Poly(galactose methacrylate).

A quantity of 306 mg of poly(galactose methacrylate), prepared as described in Example 1, was dissolved in 27 ml of dimethylformamide, 3 ml of glacial acetic acid and 3 ml of freshly distilled phenylhydrazine were added, and after 24 hr. at 20° in the dark the yellow solution was added dropwise to 300 ml of water. The pale-yellow polymer phenylhydrazone (VIII) was washed thoroughly with water and dried. It weighed 357 mg (85.6% yield) and was insoluble. Anal.: C, 55.4; H, 6.62; N, 8.2. Calc. for $(C_{16}H_{22}N_2O_6)_n$: C, 56.8; H, 6.56; N, 8.3%.

Preparation of Phenyllosazone of Poly(galactose methacrylate).

A quantity of 204 mg of poly(galactose methacrylate) was dissolved in 20 ml of water, the solution heated to 90°, and 0.2 ml of glacial acetic acid and 0.35 ml of freshly distilled phenylhydrazine were added with vigorous stirring, when a precipitate separated almost immediately. The mixture was stirred at 90° for 2 hr., cooled, and the orange product washed with ethanol and ether. The orange powder weighed 248 mg and was quite insoluble in the normal range of solvents. Anal.: C, 58.7; H, 6.54; N, 10.3. Calc. for a polymer containing two units of phenylhydrazone (VIII) for each phenyllosazone unit, i.e. $[(C_{16}H_{22}N_2O_6)_2 \cdot C_{22}H_{20}N_4O_5]_n$: C, 58.5; H, 6.40; N, 10.2%.

EXAMPLE 6.

Preparation of Phenylhydrazone of Poly(galactose acrylate).

A quantity of 102 mg of poly(galactose acrylate), prepared as described in Example 2, was dissolved in 9 ml of dimethylformamide 1 ml of glacial acetic acid and 1 ml of freshly distilled phenylhydrazine were added, and after 24 hr. at 20° in the dark the solution was added dropwise to 100 ml of water. The pale-yellow polymer phenylhydrazone (IX) was washed with water, ethanol and ether to yield 120 mg (85% yield), which was insoluble in the normal range of solvents. Anal.: C, 54.0; H, 6.37; N, 8.0. Calc. for $(C_{15}H_{20}N_2O_6)_n$: C, 55.6; H, 6.62; N, 8.6%.

Preparation of Phenyllosazone of Poly(galactose acrylate).

A quantity of 0.1 g of poly(galactose acrylate) was dissolved in 10 ml of water, the solution heated to 90°, and 0.1 ml of glacial acetic acid and 0.2 ml of freshly distilled phenylhydrazine were added with vigorous stirring. After 2 hr. at 90°, the mixture was cooled, and the orange phenyllosazone washed with water, ethanol and ether. It weighed 136 mg and was quite insoluble. Anal.: C, 58.9; H, 6.16; N, 10.4. Calc. for a polymer containing two units of phenylhydrazone (IX) for each phenyllosazone unit, i.e. $[(C_{15}H_{20}N_2O_6)_2 \cdot C_{21}H_{24}N_4O_5]_n$: C, 57.6; H, 6.26; N, 10.5%.

EXAMPLE 7.

Preparation of Poly(6-O-methacryloyl-D-galactonic acid) (X) and its 1,4-Lactone (XI).

0.991 g of poly(galactose methacrylate), prepared as described in Example 1, was dissolved in 50 ml of 4 M-acetic acid, 40 ml of M-sodium chlorite added, the solution diluted to 100 ml with water, and the oxidation allowed to proceed at 20° for 24 hr. Acetic acid and inorganic material were removed by dialysis, first against running tap-water and then against distilled-water, and cations were removed by passage through an Amberlite resin IR-120-H column ("Amberlite" is a Registered Trade Mark). The eluate and water washings gave 170 ml of a colourless solution containing the polymer acid (X). The solution was divided into two 85 ml portions.

One portion was freeze-dried to yield a white powder, weighing 330 mg, which

was dried *in vacuo* over phosphoric oxide at 17° for 18 hr. It had $[\alpha]_D - 36^\circ$ after 5 days in water (0.491 g/100 ml), which indicated appreciable conversion into the polymeric 1,4-lactone (XI). The inherent viscosity was 7.4 dl/g (0.115 g/100 ml in water). Complete conversion into the lactone (XI) was effected by drying the powder *in vacuo* over phosphoric oxide at 60°. The product was now insoluble in water, and its infrared spectrum showed strong absorption at 1780 cm^{-1} , which is characteristic of a 1,4-lactone structure. Anal.: C, 48.9; H, 5.93. Calc. for $(\text{C}_{11}\text{H}_{14}\text{O}_7)_n$: C, 48.8; H, 5.73%. The polyacid (X) is thus converted into its lactone (XI) during isolation and drying, and the extent of lactonisation is dependent on the drying conditions.

Preparation of Poly(sodium-6-O-methacryloyl-D-galactonate).

The second 85 ml portion of poly(6-O-methacryloyl-D-galactonic acid) (X) from the above preparation was titrated to pH 9 with 20 ml of 0.1 N-sodium hydroxide, and the solution dialysed against distilled water for 24 hr. The solution was then concentrated and freeze-dried to yield the sodium salt as a monohydrate, weighing 350 mg and having $[\alpha]_D + 17^\circ$ (0.5 g/100 ml in water). It possessed a high inherent viscosity (14.9 dl/g) in water (0.1 g/100 ml), which was reduced to 2.2 dl/g in 0.1 M-sodium chloride (0.1 g/100 ml). This behaviour is typical of high-molecular-weight polyelectrolytes, such as sodium alginate, sodium pectate, carrageenan, and many other gums and mucilages containing acidic functions. Anal.: C, 39.0; H, 6.01; Na, 7.6. Calc. for $(\text{C}_{10}\text{H}_{13}\text{NaO}_6\cdot\text{H}_2\text{O})_n$: C, 39.5; H, 5.63; Na, 7.6%. The sodium salt was converted into water-insoluble salts on treatment with a range of metal cations, including silver, calcium, barium, copper, lead, and ferric, and the preparation of the calcium salts is described below.

Preparation of Poly(calcium-6-O-methacryloyl-D-galactonate).

A volume of 10 ml of 1% calcium chloride solution was added dropwise to 10 ml of an aqueous solution of 51 mg of the above polymeric sodium salt, when a white flocculent precipitate immediately separated. This was washed with water, ethanol and ether to give the calcium salt as a white powder, weighing 50.7 mg. Anal.: Ca, 6.2. Calc. for $(\text{C}_{10}\text{H}_{13}\text{CaO}_6)_n$: Ca, 7.1%. Other insoluble metal salts were prepared similarly.

EXAMPLE 8.

Preparation of Poly(6-O-acryloyl-D-galactonic acid) (XII) and its 1,4-Lactone (XIII).

0.504 g of poly(galactose acrylate), prepared as described in Example 2, was dissolved in 25 ml of 4 M-acetic acid, 20 ml of M-sodium chlorite added, the solution diluted to 50 ml with water, and the oxidation allowed to proceed at 20° for 24 hr. The solution was worked up as described above for the methacrylate to yield 132 ml of a solution containing the polymer acid (XII). This was again divided into two 66 ml portions.

One portion was concentrated and freeze-dried to give a white powder, weighing 201 mg, which was dried *in vacuo* over phosphoric oxide at 17° for 18 hr. Its specific rotation was -17° in water (0.5 g/100 ml), which showed that some of the carboxylic acid groups had been converted into the 1,4-lactone. Complete lactonisation was effected by drying at 60° for 24 hr., when the infrared spectrum showed a strong absorption band at 1780 cm^{-1} . The product was now the polymeric lactone (XIII). Anal.: C, 45.9; H, 5.37. Calc. for $(\text{C}_9\text{H}_{12}\text{O}_7)_n$: C, 46.6; H, 5.21%. The lactone was insoluble in water.

Preparation of Poly(sodium 6-O-acryloyl-D-galactonate).

The second 66 ml portion of the above polyacid (XII) was titrated to pH 9 with 0.1 N-sodium hydroxide and the viscous solution dialysed against distilled water. The solution was concentrated and freeze-dried to give the sodium salt as a white powder, weighing 294 mg and having $[\alpha]_D + 10^\circ$ (0.5 g/100 ml in water). Its inherent viscosity in water was 12.2 dl/g (0.1 g/100 ml), which was reduced to 1.4 dl/g in 0.1 M-sodium chloride (0.1 g/100 ml). Anal.: C, 40.8; H, 5.73; Na, 5.6. Calc. for $(\text{C}_{10}\text{H}_{13}\text{NaO}_6\cdot\text{H}_2\text{O})_n$: C, 37.3; H, 5.21; Na, 7.9%. The properties of this compound were similar to those of the methacrylate polymer described in Example 7. Its silver, calcium, barium, copper, lead, and ferric salts were insoluble in water.

EXAMPLE 9.

Preparation of Poly(6-O-methacryloyl-D-galactitol) (XIV).

0.5 g of poly(galactose methacrylate), prepared as described in Example 1, was dissolved in 45 ml of water, the solution cooled to 0°, and sodium borohydride, 152 mg dissolved in 5 ml of water, added dropwise with stirring. After 24 hr. at 20°, the solution was acidified with acetic acid, dialysed for 24 hr., concentrated and freeze-dried to yield the reduced product (XIV) as a white powder, weighing 419 mg (83.1% yield) and having $[\alpha]_D + 15^\circ$ (0.5 g/100 ml in water). Its inherent viscosity was 2.7 dl/g (0.5 g/100 ml in water). The compound was non-reducing to Fehling solution. Anal.: C, 47.9; H, 7.20. Calc. for $(C_{10}H_{14}O_7)_n$: C, 48.0; H, 7.25%.

Nitration of Poly(6-O-methacryloyl-D-galactitol) (XIV).

A quantity of 152 mg of the above reduced product (XIV) was nitrated with nitrogen pentoxide in chloroform exactly as described in Example 3 for poly(galactose methacrylate). The ester, weighing 244 mg (93.5% yield), was a white powder, which analysed as a tetranitrate. Anal.: C, 26.9; H, 3.26; N, 13.4. Calc for $(C_{10}H_{14}N_4O_{15})_n$: C, 27.9; H, 3.28; N, 13.0%. 40% of the product was soluble in ethyl acetate, the remainder forming a clear, insoluble gel.

The above reactions carried out with the polymers poly(galactose 6-methacrylate) and poly(galactose 6-acrylate) indicate, in general, that they are much more reactive than natural polysaccharides.

The commercial usefulness of natural polysaccharides containing carboxylic acid groups is well established, e.g. pectin, alginic acid, and the natural gums and mucilages (cf. "Industrial Gums", R. L. Whistler and J. N. Bemiller, editors, 1959, Academic Press: New York). The polymers of the present invention can be readily converted into polyacids and polylactones as shown in the examples. A recent attempt has been made by Khomyakov et al. (Vysokomolekul. Soedin., 1965, 7 1030) to increase the reactivity of dextran by introducing aldehyde and carboxyl groups by periodate oxidation followed by chlorite oxidation. Many other examples of this type of reaction with natural polysaccharides can be cited.

On the other hand, the reduced polymer, poly(6-O-methacryloyl-D-galactitol), will be much more stable than the aldehydic polymer, and this could be an advantage in some cases.

The polyphenylhydrazones and polyphenylosazones might be useful chelating agents.

The raw material for the preparation of the compounds of this invention, i.e., galactose is prepared from lactose or milk sugar, which is a by-product from cheese production and is obtained from whey as a crystalline solid of greater than 99% purity. Lactose is used to a limited extent in food and drug preparations but is not used to any extent as an intermediate in the chemical industry. The utilisation of galactose in synthetic polymer production is thus a great benefit to the milk industry and greatly increases the value of whey.

The compounds of galactose prepared by the present invention are superior to the glucose compounds described in U.S. Patent No. 3,103,508. This is due to the galactose monomers being obtainable in a well-defined, highly pure crystalline state, which fact would not be obvious to anyone skilled in the art and required extensive investigation into their preparation. The aforesaid crystalline characteristics enables polymers of higher molecular weight to be obtained.

WHAT WE CLAIM IS:—

1. A method of preparing a polymer from esters of α,β olefinically unsaturated polymerisable mono- and di-carboxylic acids and galactose comprising reacting a ketone with galactose to form a 1,2:3,4 diketal, forming an ester of said diketal and an α,β olefinically unsaturated polymerisable mono- or di-carboxylic acid, polymerising said ester in the presence of a free radical catalyst and finally removing the diketal residues from the polymerised product by controlled hydrolysis.

2. A method according to claim 1 wherein the ketone is acetone, methyl ethyl ketone, methyl propyl ketone, mono-chloracetone or cyclohexanone.

3. A method according to claim 1 or 2 wherein the olefinically α,β unsaturated mono- or di-carboxylic acid is acrylic, methacrylic, α -chloracrylic, α -cyanoacrylic, maleic, half esters of maleic, fumaric, half esters of fumaric, α -ethacrylic, itaconic or half esters of itaconic acid.

4. A method according to any one of the preceding claims wherein the controlled hydrolysis is effected by dissolving the polymerised product in an organic acid and diluting the solution gradually with water.

5. A method according to claim 4 wherein the organic acid is formic acid.
6. A method according to any one of the preceding claims wherein the free radical catalyst is azobisisobutyronitrile.
7. A method according to any one of the preceding claims wherein the diketal is reacted with a lower hydrocarbon ester of the α,β olefinically unsaturated mono- or di-carboxylic acid in the presence of a vinyl polymerisation inhibitor and a catalyst and the hydrocarbon alcohol is distilled off as it is formed.
8. A method according to any one of claims 1 to 6 wherein the ester is prepared by reacting the diketal with an anhydride of the α,β olefinically unsaturated mono- or di-carboxylic acid.
9. A polymer of an ester between the hydroxy group in the six position of galactose and an α,β olefinically unsaturated mono- or di-carboxylic acid.
10. Poly(diisopropylidene galactose 6-methacrylate).
11. Poly(diisopropylidene galactose 6-acrylate).
12. Poly(galactose 6-methacrylate).
13. Poly(galactose 6-acrylate).
14. The acetate of poly(galactose 6-methacrylate).
15. The benzoate of poly(galactose 6-methacrylate).
16. The phenylcarbamate of poly(galactose 6-methacrylate).
17. The nitrate of poly(galactose 6-methacrylate).
18. The phenylhydrazone of poly(galactose 6-methacrylate).
19. The phenylosazone of poly(galactose 6-methacrylate).
20. The acetate of poly(galactose 6-acrylate).
21. The benzoate of poly(galactose 6-acrylate).
22. The phenylcarbamate of poly(galactose 6-acrylate).
23. The phenylhydrazone of poly(galactose 6-acrylate).
24. The phenylosazone of poly(galactose 6-acrylate).
25. Poly(6-O-methacryloyl-D-galactonic acid) and the 1,4-lactone thereof.
26. Poly(sodium 6-O-methacryloyl-D-galactonate).
27. Poly(calcium 6-O-methacryloyl-D-galactonate).
28. Poly(6-O-acryloyl-D-galactonic acid) and the 1,4-lactone thereof.
29. Poly(sodium-6-O-acryloyl-D-galactonate).
30. Poly(6-O-methacryloyl-D-galactitol).
31. The nitrate of poly(6-O-methacryloyl-D-galactitol).
32. A polymerisable ester between the hydroxyl group in the six position of galactose and an α,β olefinically unsaturated polymerisable mono- or di-carboxylic acid.
33. A polymerisable ester according to claim 32 wherein the α,β olefinically unsaturated mono- or di-carboxylic acid is acrylic, methacrylic, α -chloracrylic, α -cyanoacrylic, maleic, half esters of maleic, fumaric, half esters of fumaric, α -ethacrylic, itaconic or half esters of itaconic acid.
34. Diisopropylidene galactose 6-methacrylate.
35. Diisopropylidene galactose 6-acrylate.
36. A method of preparing a polymerisable ester of galactose and an α,β olefinically unsaturated polymerisable aliphatic mono- or di-carboxylic acid comprising reacting a ketone with galactose to form 1,2:3,4 diketal and thereafter reacting said diketal with an α,β olefinically unsaturated polymerisable aliphatic mono- or di-carboxylic acid.
37. A method of preparing a polymer from esters of α,β olefinically unsaturated polymerisable aliphatic mono- or di-carboxylic acids and galactose and derivatives of said polymer substantially as hereinbefore described with reference to the Examples.
38. Polymers of esters of α,β olefinically unsaturated polymerisable aliphatic mono- or di-carboxylic acids and galactose and derivatives of said polymers whenever prepared by the methods of any one of claims 1 to 8 and claim 37.

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